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| 10/719,695 | 11/21/2003 | Leong Ng | ISA-012.01 | 1345 |

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| EXAMINER | |
|---|---|
| ROONEY, NORA MAUREEN | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/719,695 | NG, LEONG | |
| | Examiner | Art Unit | |
| | NORA M. ROONEY | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,16 and 22-30* is/are pending in the application.

4a) Of the above claim(s) *22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 16 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/11/2008 has been entered.

2. Claims 1-7, 16 and 22-30 are pending.

3. Claims 22-25 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/14/2006.

4. Claims 1-7, 16 and 26-30 are currently under examination as they read on a method for detectingan increased risk of heart disease.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 16 and 26-30 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method for determining an increased risk of heart

disease in a mammalian subject, comprising (a) contacting a bodily fluid sample with an antibody specific for SEQ ID NO: 2 in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease; wherein heart disease is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm, or peripheral vascular disease; wherein the bodily fluid is plasma; wherein the method comprises an immunoassay; wherein the immunoassay is a lateral flow immunoassay; wherein the immunoassay is a flow-through immunoassay; wherein the antibody specific for ORP150 is a monoclonal antibody; wherein the level of ORP150 is monitored periodically; the method of claim 1, further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease; wherein the second marker is a natriuretic peptide; wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease; wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one or more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease; and wherein the level of the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample; the specification does

not provide reasonable enablement for: a method for determining an increased risk of heart disease in a mammalian subject, comprising (a) contacting a bodily fluid sample with **an antibody specific for an oxygen related protein 150 (ORP150) comprising SEQ ID NO: 2** in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease of claims 1-7, 16 and 26-30. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses a method for determining an increased risk of heart disease in

a mammalian subject, comprising (a) contacting a bodily fluid sample with an antibody specific SEQ ID NO: 2 in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease.

The specification has not adequately disclosed a method for detecting ORP150 in a bodily fluid using antibodies to an oxygen related protein "comprising" the 13 amino acid peptide of SEQ ID NO:2. The claims, as recited, encompass the use of antibodies to detect ORP150 that are specific for portions of the oxygen related protein other than disclosed SEQ ID NO:2. The art of Lerner et al. (PTO-892; Reference U) teaches that an antibody binding epitope may be as small as 6-15 amino acid residues (In particular, whole document). Therefore, it is unpredictable whether antibodies to other undisclosed portions of ORP150 other than SEQ ID NO:2 will cross-react with and detect proteins other than ORP150. As such, one of ordinary skill in the art would be required to perform undue experimentation to practice the claimed method commensurate in scope with the claims.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and

the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 1-7, 16 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method for determining an increased risk of heart disease in a mammalian subject, comprising (a) contacting a bodily fluid sample with an antibody specific for SEQ ID NO: 2 in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease; wherein heart disease is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm, or peripheral vascular disease; wherein the bodily fluid is plasma; wherein the method comprises an immunoassay; wherein the immunoassay is a lateral flow immunoassay; wherein the immunoassay is a flow-through immunoassay; wherein the antibody specific for ORP150 is a monoclonal antibody; wherein the level of ORP150 is monitored periodically; the method of claim 1, further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease; wherein the

second marker is a natriuretic peptide; wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease; wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one or more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease; and wherein the level of the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample.

Applicant is not in possession of: a method for determining an increased risk of heart disease in a mammalian subject, comprising (a) contacting a bodily fluid sample with **an antibody specific for an oxygen related protein 150 (ORP150) comprising SEQ ID NO: 2** in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease of claims 1-7, 16 and 26-30.

Applicant has disclosed only a method for determining an increased risk of heart disease in a mammalian subject, comprising (a) contacting a bodily fluid sample with an antibody specific for SEQ ID NO: 2 in order to detect the level of ORP150 in the bodily fluid sample, and (b) comparing the level of ORP 150 in the bodily fluid sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence

of heart disease being (a) the level of ORP150 from one or more mammalian subjects free from heart disease, or (b) a previously determined reference range for ORP 150 in mammalian subjects free from heart disease; therefore, the skilled artisan cannot envision all the contemplated antibody and method possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath

at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-5, 7, 16 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Karl et al. (IDS document filed on 06/16/2004; Reference AJ).

Tsukamoto et al. teaches a method for determining atherosclerosis in a human subject, comprising (a) contacting aorta samples with a monoclonal antibody specific for an oxygen related protein 150 (ORP150) comprising instant SEQ ID NO: 2 in order to detect the level of ORP150 in the aorta sample, and (b) comparing the level of ORP 150 in the aorta sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being the level of ORP150 from humans free from heart disease (control patients); and wherein the method comprises an immunoassay (In

particular, paragraph spanning pages 1931-32; paragraph spanning columns on page 1935, whole document). The reference also teaches that atherosclerosis patients have endogenous anti-ORP150 antibody in their serum as measured by ELISA (In particular, page 1932, right column second full paragraph; page 1937 to the 'Discussion' section, whole document).

The claimed invention differs from the prior art in the recitation of detecting ORP150 "in a bodily fluid sample" of claim 1; "wherein the bodily fluid sample is plasma" of claim 3; "wherein the immunoassay is a lateral flow immunoassay" of claim 5; "wherein the immunoassay is a flow through immunoassay of claim 6; "wherein the level of ORP150 is monitored periodically" of claim 16; "further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease" of claim 26; "wherein the second marker is a natriuretic peptide" of claim 27; "wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease" of claim 28; "wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one ore more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease" of claim 29; and "wherein the level of the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample" of claim 30.

It would have been obvious to one of ordinary skill in the art at the time of invention to detect ORP150 in the plasma because bodily fluids such as blood, serum and plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for

performing an immunoassay. In addition, Tsukamoto et al specifically teaches that atherosclerosis patients have ORP150 in aortic samples and endogenous anti-ORP150 antibody in their plasma, so it would be obvious to measure ORP150 in bodily fluids such as plasma and serum, particularly because of the convenience in obtaining blood, serum and plasma samples.

Karl et al. teaches immunoassay reagents and methods for measurement of natriuretic peptides in blood and plasma for diagnosis of cardiac disease (In particular, abstract, introduction, and page 180, last paragraph). The reference teaches using a sandwich assay, which is a lateral flow immunoassay as defined in the instant specification, to detect natriuretic peptide NT-proBNP to monitor cardiac disease and therapy. Karl et al teaches that sandwich format immunoassays, are efficient "highly sensitive" and "specific" (In particular, page 177, abstract).

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein in a patient's aorta sample with detection of ORP 150 in a bodily fluid sample such as plasma in a lateral flow immunoassay and to compare the amount to a healthy control to detect increased risk of heart disease and to monitor disease periodically because, as taught by Karl et al., sandwich format immunoassays, are efficient " highly sensitive" and "specific" (In particular, page 177, abstract) and because bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of natriuretic peptide second markers in a patient's bodily fluid, such as plasma, using antibodies to the natriuretic peptide second markers with detection of ORP150 in a lateral flow immunoassay to detect increased risk heart disease. Lateral flow immunoassays, such as sandwich format immunoassays, are efficient "highly sensitive" and "specific" (In particular, page 177, abstract). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 and BNP or N-BNP natriuretic peptides with a lateral flow immunoassay because it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Claims 1-5, 7, 16 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Hall et al. (IDS filed on 6/18/2004, Reference AG).

Tsukamoto et al. teaches a method for determining atherosclerosis in a human subject, comprising (a) contacting aorta samples with a monoclonal antibody specific for an oxygen related protein 150 (ORP150) comprising instant SEQ ID NO: 2 in order to detect the level of ORP150 in the aorta sample, and (b) comparing the level of ORP 150 in the aorta sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being the level of ORP150 from humans free from heart disease (control patients); and wherein the method comprises an immunoassay (In particular, paragraph spanning pages 1931-32; paragraph spanning columns on page 1935, whole document). The reference also teaches that atherosclerosis patients have endogenous anti-ORP150 antibody in their serum as measured by ELISA (In particular, page 1932, right column second full paragraph; page 1937 to the 'Discussion' section, whole document).

The claimed invention differs from the prior art in the recitation of detecting ORP150 "in a bodily fluid sample" of claim 1; "wherein the bodily fluid sample is plasma" of claim 3; "wherein the immunoassay is a lateral flow immunoassay" of claim 5; "wherein the immunoassay is a flow through immunoassay of claim 6; "wherein the level of ORP150 is monitored periodically" of claim 16; "further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease" of claim 26; "wherein the second marker is a natriuretic peptide" of claim 27; "wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease" of claim 28;

"wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one ore more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease" of claim 29; and "wherein the level of the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample" of claim 30.

Hall et al. teaches detection of natriuretic peptide, particularly N-terminal pro-brain natriuretic peptide and brain natriuretic peptide, in the diagnosis, management and periodic monitoring of heart failure patients by comparing the amounts to healthy control patients. The reference teaches that the determinations should be combined with other diagnostic examinations, including other peptide determinations to improve diagnostic performance and that it can be done over a series of time points to better monitor disease (In particular, page 395, fourth paragraph, page 396, fourth paragraph and page 397, last paragraph). The reference also teaches the ease of detecting the proteins in a patient's plasma (In particular, page 395, third paragraph and page 396, first and last paragraphs) and detection by immunoassay (In particular, pages 395, second paragraph).

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine the determination of ORP 150 with the determinations of other diagnostic markers, such as natriuretic peptides, for diagnosis of heart failure in view of the suggestion in Hall et al. to combine tests to improve diagnostic performance. It would also be obvious to one

of ordinary skill in the art at the time the invention was made to detect the level of ORP 150 alone or in combination with a second marker to better adjust a patient's therapy according to their cardiac disease and severity associated peptide levels, as suggested by Hall et al. (In particular, page 396, third paragraph and page 396, second paragraph). It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Claims 1-4 and 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of May et al. (PTO-892 mailed on 07/11/2007; Reference A).

Tsukamoto et al. teaches a method for determining atherosclerosis in a human subject, comprising (a) contacting aorta samples with a monoclonal antibody specific for an oxygen related protein 150 (ORP150) comprising instant SEQ ID NO: 2 in order to detect the level of ORP150 in the aorta sample, and (b) comparing the level of ORP 150 in the aorta sample with

the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being the level of ORP150 from humans free from heart disease (control patients); and wherein the method comprises an immunoassay (In particular, paragraph spanning pages 1931-32; paragraph spanning columns on page 1935, whole document). The reference also teaches that atherosclerosis patients have endogenous anti-ORP150 antibody in their serum as measured by ELISA (In particular, page 1932, right column second full paragraph; page 1937 to the 'Discussion' section, whole document).

The claimed invention differs from the prior art in the recitation of detecting ORP150 "in a bodily fluid sample" of claim 1; "wherein the bodily fluid sample is plasma" of claim 3; and detection of ORP 150 "wherein the immunoassay is a flow-through immunoassay" of claim 6.

May et al. teaches a specific, flow-through immunoassay for determining pregnancy that reacts a liquid biological sample with a test strip made of dry porous material that absorbs the liquid biological sample and transports the biological sample to a membrane zone with immobilized antibody to hCG. If the antigen is present in a biological sample, a colored spot develops on the surface of the membrane through use of a color tagged secondary antibody. (In particular, Claims 1-34 and column 2 lines 3-20).

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein in a patient's bodily fluid, such as plasma, using monoclonal antibodies to the ORP 150 protein in a flow-thorough immunoassay to detect increased risk of heart disease. The May et al. reference teaches that such a device is optimal as it is specific, reliable, quick, convenient, commercially available and suitable for home-use

because of the lack of requisite skill and ease of obtaining a bodily fluid sample for use (In particular column 1 lines 10-45 and lines 64-67 and column 2, lines 1-2). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 11, 2009

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644